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Programmed Ventricular Stimulation in Patients With Left Ventricular Dysfunction and Ventricular Tachycardia: Effects of Acute Hemodynamic Improvement Due to Nitroprusside

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To assess the electrophysiologic effects of acute hemodynamic improvement in patients with left ventricular systolic dysfunction, 12 patients with a left ventricular ejection fraction <0.40 and a history of sustained monomorphic ventricular tachycardia were studied. All patients had underlying coronary artery disease. Patients underwent programmed cardiac stimulation in random order during a baseline period and with nitroprusside infusion. Mean pulmonary capillary wedge pressure decreased from 20 ± 8 mm Hg at baseline study to 8 ± 3 mm Hg during nitroprusside infusion ($p < 0.0001$). Pulmonary artery, right atrial and systemic arterial pressures also decreased with nitroprusside ($p < 0.01$). Cardiac output did not change. Left ventricular dimensions, determined by two-dimensional echocardiography, decreased significantly during nitroprusside infusion.

The right ventricular effective refractory period, measured during ventricular drive trains at cycle lengths of 400 and 600 ms, were similar during baseline and nitroprusside periods (271 ± 30 versus 274 ± 31 ms at 600 ms, and 249 ± 25 versus 246 ± 18 ms at 400 ms). In 2 patients no ventricular arrhythmias were induced during either study period; in the other 10, ventricular tachyarrhythmias were induced during both periods. The mean number of extrastimuli required to induce a ventricular tachyarrhythmia was similar during the baseline period (1.8 ± 0.6) and during nitroprusside infusion (1.9 ± 0.7). As well, the mean cycle length of ventricular tachycardia induced was similar during the baseline period (347 ± 61 ms) and during nitroprusside infusion (342 ± 70 ms).

Thus, in patients with left ventricular systolic dysfunction and ventricular tachycardia due to coronary artery disease, acute hemodynamic improvement with a reduction in left ventricular size does not affect characteristics of ventricular tachycardia induction. Determination of whether long-term vasodilator treatment affects these characteristics requires further study.

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Clinical studies have demonstrated an association between heart failure and the occurrence of ventricular tachyarrhythmias. Up to 87% of patients with heart failure have complex ventricular ectopic activity (1). The frequency and complexity of ventricular arrhythmias are related to mortality and the severity of congestive heart failure (2–7). Furthermore, approximately 50% of deaths in patients with congestive heart failure occur suddenly, suggesting an arrhythmic origin (8). Proarrhythmic factors associated with rhythm disturbances in congestive heart failure include left ventricular dysfunction and segmental wall motion abnormalities (3–9). Changes in ventricular muscle length and tension associated with these factors may induce electrophysiologic abnormalities that predispose to arrhythmias (10–16). Two studies (17,18) demonstrated that vasodilators increased survival rates in patients with heart failure. Two other studies (19,20) showed that patients with heart failure have less ventricular ectopic activity while taking an angiotensin-converting enzyme inhibitor.

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Table 1. Characteristics of the 15 Study Patients

Patient No.*	Age (yr)/ Gender	Diseased Vessel†	LVEF	RWMA	Antiarrhythmic Drug	Order of Study Periods
1	48/M	LAD, RCA	0.09	Apical akinesia	Amiodarone	B, N
2	41/M	LAD, LCx, RCA	0.31	Septal dyskinesia, anterior akinesia	Procainamide	N, B
3	48/F	LAD	0.25	Anteroapical akinesia	Quinidine	N, B
4	63/M	LAD	0.31	Apical dyskinesia	Quinidine	B, N
5	62/M	LAD, LCx, RCA	0.31	Apical akinesia	Sotalol	B, N
6	68/F	LAD	0.25	Apical dyskinesia, anterior akinesia	Sotalol	N, B
7	65/M	LAD, LCx, RCA	0.10	Anteroapical and inferior akinesia	Procainamide	B, N
8	49/M	LAD, RCA	0.29	Anteroapical dyskinesia	Amiodarone	B, N
9	50/M	LCx, RCA	0.35	Inferoapical akinesia	Sotalol	B, N
10	66/M	LAD, LCx, RCA	0.33	Septal dyskinesia, apical akinesia	Sotalol	B, N
11	66/M	LCx	0.24	Posterior akinesia	Quinidine, mexiletine	N, B
12	63/M	RCA	0.27	Inferoposterior akinesia	Sotalol	B, N
13	53/M	LAD	0.23	Anteroapical dyskinesia	None	B
14	60/M	LAD, LCx, RCA	0.12	Apical dyskinesia, anterior and inferior akinesia	Procainamide, tocainide	N
15	52/M	LCx, RCA	0.24	Inferoapical akinesia	Sotalol	B

*Patients are listed in chronological order, except for Patients 13, 14 and 15, who were excluded from analysis after induction of ventricular fibrillation in the initial study period. Patients 1 through 12 in subsequent tables correspond to Patients 1 through 12 in this table. †A vessel was judged to be diseased if ≥70% diameter stenosis was present on coronary angiography. B = baseline; F = female; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LVEF = left ventricular ejection fraction; M = male; N = nitroprusside; RCA = right coronary artery; RWMA = regional wall motion abnormalities (akinesia or dyskinesia).

Although the association between heart failure and ventricular arrhythmias is evident, no study has assessed whether an acute improvement in the hemodynamic state decreases the susceptibility to these arrhythmias. The purpose of this study was to determine whether acute hemodynamic improvement with reduction in ventricular size affects the induction of ventricular tachycardia in patients with sustained monomorphic ventricular tachycardia and left ventricular dysfunction.

To bring about such acute changes in pressures and volumes, we administered nitroprusside, a rapid-acting "pure" vasodilator without known direct myocardial effects. We specifically sought to determine whether the efficacy (or lack of efficacy) of antiarrhythmic drugs is influenced by such acute hemodynamic changes.

Methods

Study patients (Table 1). Criteria for entry into the study were a history of spontaneous sustained monomorphic ventricular tachycardia, a history of heart failure and a left ventricular ejection fraction (as determined by cineventriculography or gated blood pool scanning) <0.40. Fifteen patients (13 men and 2 women, age 57 ± 9 years) were enrolled. All had coronary artery disease, had experienced at least one prior myocardial infarction and had associated left ventricular segmental wall motion abnormalities. Three patients (Patients 2, 3 and 6) had undergone left ventricular aneurysmectomy. The mean left ventricular ejection fraction was 0.25 ± 0.08. No patient had clinically decompensated heart failure at the time of study. Until 24 hours before study, two patients were taking nitrates, 3 were taking nitrates and captopril, 1 was taking nifedipine, 1 was taking nitrates and diltiazem, and eight were taking no vasodilators. The six patients who had been taking vasodilators did not respond differently to programmed stimulation from the eight patients who had not been taking vasodilators.

All 15 patients were in sinus rhythm and had had sustained monomorphic ventricular tachycardia induced during a previous electrophysiologic study while taking no antiarrhythmic drugs. At the time of entry into the protocol, all but one patient were being treated with antiarrhythmic drugs. The protocol was approved by the Subcommittee for Human Studies, Committee on Research, Massachusetts General Hospital on August 26, 1985, and all subjects gave written informed consent.

Study protocol. Digoxin, diuretic drugs and vasodilator drugs were discontinued 24 h before the study, but antiarrhythmic drugs were administered as scheduled. Studies were performed with the patient under mild sedation (diazepam, 5 to 10 mg orally) and local anesthesia with 1% lidocaine. A 5F introducer was placed in the femoral artery

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to measure systemic arterial pressure. Under fluoroscopic guidance, a 7F balloon-tipped thermodilution Swan-Ganz catheter was introduced percutaneously through the right femoral vein and advanced to the pulmonary artery. A 6F quadripolar electrode catheter was introduced percutaneously through the right femoral vein and advanced to the right ventricular apex, and ventricular capture was confirmed. When ventricular tachycardia could not be induced from the right ventricular apex, the catheter was advanced to the outflow tract and stimulation was performed from that site.

Patients were randomly assigned to undergo the initial electrophysiologic study during either the baseline period or nitroprusside infusion (Table 1). Intravenous sodium nitroprusside was begun at 25 μg/min, and the dosage increased at 5 min intervals until the pulmonary capillary wedge pressure had decreased to approximately 50% of its baseline value. In patients randomized to undergo the first programmed stimulation study during nitroprusside infusion, pressures were measured before nitroprusside was infused. After discontinuation of the nitroprusside infusion, systemic arterial and pulmonary capillary wedge pressures were allowed to return to baseline values for at least 10 min before the electrophysiologic study was repeated.

Mean and phasic systemic arterial, pulmonary capillary wedge, pulmonary artery and right atrial pressures were measured just before electrophysiologic studies in the baseline and nitroprusside periods. Cardiac output was determined by the thermodilution method. Systemic arterial blood was sampled for oxygen saturation and central venous blood for fractionated plasma catecholamine concentration immediately before each electrophysiologic study. Two-dimensional echocardiography, including parasternal long- and short-axis and apical two and four chamber views, was performed before each of the two electrophysiologic studies in eight patients. Surface electrocardiographic (ECG) leads I and aVF, the right ventricular local electrogram, systemic arterial pressure and pulmonary artery pressure were continuously monitored and recorded on a multichannel oscilloscopic recorder (VR-16, Electronics for Medicine). Bandpass filters were set at 30 and 500 Hz, and recordings were made at 100 mm/s. Systemic arterial oxygen saturation was measured with an oximeter (Radiometer, Copenhagen OSM2). Plasma epinephrine and norepinephrine concentrations were determined by radioimmunoassay (Smith Kline Bio-Science Laboratories) (21).

Programmed stimulation protocol. Diastolic threshold was determined at each ventricular stimulation site immediately before programmed cardiac stimulation during both the baseline and the nitroprusside infusion study. Programmed stimulation was performed at the right ventricular apex with use of a programmable stimulator (model DTU 210, Bloom Associates Ltd.) that introduced 2 ms rectangular pulses at twice diastolic threshold. The stimulation protocol included single, double and triple extrastimuli, as previously described (22). Baseline and nitroprusside stimulation studies were performed without a change of electrode catheter position between the two trials. Programmed single and double extrastimuli were introduced during ventricular pacing after eight beat drive trains at cycle lengths of 400 and 600 ms. Triple extrastimuli were introduced after an eight beat drive train at a cycle length of 400 ms. The coupling intervals were decreased by 10 ms decrements until refractoriness was encountered. The right ventricular effective refractory period was also measured using a single extrastimulus after an eight beat drive train. The reproducibility of the measurement was confirmed in each case by repeating the programmed stimulation at coupling intervals immediately before and when the ventricle was refractory to stimulation.

The programmed stimulation protocol had three possible end points: 1) induction of sustained ventricular tachyarrhythmia, defined as lasting >100 beats or requiring intervention before that time because of hemodynamic deterioration; 2) reproducible induction of nonsustained ventricular tachycardia, defined as a run of ≥10 consecutive ventricular complexes lasting <30 s and terminating spontaneously; or 3) completion of the protocol without induction of ventricular tachyarrhythmia.

A 12 lead surface ECG was obtained during each induced sustained ventricular arrhythmia. Induced ventricular tachycardia was terminated, when possible, by rapid ventricular pacing. When syncope occurred before ventricular pacing terminated the arrhythmia, direct current cardioversion using 200 J from an external defibrillator was performed. If a ventricular arrhythmia required direct current cardioversion during the initial electrophysiologic study, the protocol was discontinued and the second induction was not performed.

Data analysis. After each study, 12 lead ECGs of the ventricular tachycardias induced during the baseline period and during nitroprusside infusion were examined in blinded fashion. Ventricular tachycardias were considered morphologically identical when their mean QRS axes in both the frontal and the horizontal plane did not differ by >45°. Right and left bundle branch block mimicry was not used for morphologic classification because of the subjective nature of this criterion.

Echocardiographic images were recorded on videotape and analyzed on a Sony SMC-70G microcomputer by an investigator who was unaware of other data. End-diastolic and end-systolic images were subjected to planimetry with a lightpen, and measurements of ventricular dimensions were made.

Statistical analysis. Data are presented as mean values ± SD. Comparisons between data from the baseline and nitroprusside infusion periods were made by Student's *t* test for

Table 2. Hemodynamic and Neuroendocrine Measurements in 12 Patients

Patient No.	Study Period	PCW (mm Hg)	PA (mm Hg)	RA (mm Hg)	MAP (mm Hg)	CO (liters/min)	Plasma NE (pg/ml)	Plasma Epi (pg/ml)
1	B	17	29	1	100	3.9	304	112
	N	8	18	1	82	4.4	240	112
2	B	19	30	3	85	5.8	288	10
	N	5	8	2	70	7.0	492	92
3	B	24	33	4	64	5.5	364	52
	N	8	17	0	50	5.5	372	80
4	B	24	29	8	110	5.6	—	—
	N	15	17	1	93	5.1	—	—
5	B	32	39	13	102	4.2	316	420
	N	9	25	6	90	4.8	248	10
6	B	25	38	16	95	4.0	224	64
	N	4	14	0	70	3.5	648	10
7	B	32	32	15	103	3.6	144	10
	N	12	12	0	77	3.5	150	10
8	B	11	16	4	92	5.7	244	10
	N	4	10	0	75	5.3	634	96
9	B	14	20	16	90	4.9	262	10
	N	8	13	12	75	5.0	406	10
10	B	24	43	10	120	4.9	260	100
	N	9	26	12	85	5.0	524	296
11	B	9	17	8	84	4.6	248	116
	N	5	12	2	65	4.9	808	316
12	B	12	17	4	88	4.0	240	10
	N	5	10	2	54	3.0	228	10
Mean ± SD								
	B	20 ± 8	29 ± 9	9 ± 5	94 ± 14	4.7 ± 0.8	263 ± 57	83 ± 120
	N	8 ± 3	15 ± 6	3 ± 4	74 ± 13	4.7 ± 1.1	432 ± 209	95 ± 112
p<		0.0001	0.0001	0.01	0.0001	NS	0.05	NS

CO = cardiac output; Epi = epinephrine concentration; MAP = mean systemic arterial pressure; NE = norepinephrine concentration; PA = pulmonary artery pressure; PCW = pulmonary capillary wedge pressure; RA = right atrial pressure; other abbreviations as in Table 1.

paired observations; statistical significance was set at $p < 0.05$.

Results

Of the 15 patients enrolled in the study, 3 required direct current cardioversion during the first trial of programmed cardiac stimulation (Patients 13 to 15, Table 1). The protocol was terminated in these patients, and they were excluded from further analysis. Thus, the study group consisted of 12 patients, all of whom were taking antiarrhythmic drugs.

Hemodynamic and neuroendocrine measurements (Table 2). The nitroprusside infusion rate was 68 ± 42 μg/min. Mean pulmonary capillary wedge pressure decreased from 20 ± 8 mm Hg during the baseline period to 8 ± 3 mm Hg ($p < 0.0001$) during nitroprusside infusion. Mean pulmonary artery pressure decreased from 29 ± 9 to 15 ± 6 mm Hg ($p < 0.0001$), right atrial pressure from 9 ± 5 to 3 ± 4 mm Hg ($p < 0.01$) and mean systemic arterial pressure from 94 ± 14 to 74 ± 13 mm Hg ($p < 0.0001$) during nitroprusside infusion. Cardiac output did not change.

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Table 3. Echocardiographic Measurements in 12 Patients

Measurement	Baseline	Nitroprusside	p Value
Parasternal long-axis diameter (cm)			
Systole	5.16 ± 0.90	4.80 ± 0.87	<0.0001
Diastole	5.99 ± 0.98	5.61 ± 0.86	<0.01
Short-axis area (cm^2)			
Systole	21.9 ± 4.7	17.7 ± 4.1	<0.005
Diastole	28.3 ± 6.2	24.0 ± 4.4	<0.01
Apical four chamber area (cm^2)			
Systole	39.4 ± 12.4	36.7 ± 13.3	NS
Diastole	45.4 ± 13.4	42.3 ± 13.8	<0.05
Apical four chamber length (cm)			
Systole	8.70 ± 1.05	8.40 ± 1.18	NS
Diastole	9.44 ± 1.30	8.99 ± 1.31	NS
Apical two chamber area (cm^2)			
Systole	39.6 ± 13.5	36.2 ± 12.3	<0.02
Diastole	45.2 ± 15.3	41.8 ± 15.6	<0.01
Apical two chamber length (cm)			
Systole	8.74 ± 1.17	8.46 ± 1.25	NS
Diastole	9.40 ± 1.30	9.07 ± 1.25	NS

A small but statistically significant decrease in systemic arterial oxygen saturation occurred during nitroprusside infusion (0.96 ± 0.02 to 0.94 ± 0.02, $p < 0.003$). Plasma norepinephrine and epinephrine concentrations varied over a wide range during the baseline and nitroprusside periods. Mean plasma norepinephrine concentration was higher during nitroprusside infusion, whereas epinephrine concentration did not change significantly.

Echocardiographic measurements (Table 3). Left ventricular diameter measured in the parasternal long-axis view and cross-sectional area measured in the parasternal short-axis and apical two chamber views decreased during nitroprusside infusion. Left ventricular length measured in the apical two and four chamber views during diastole and systole was smaller during nitroprusside infusion, but the differences did not reach statistical significance.

Electrophysiologic measurements (Table 4). Sinus cycle length was longer during the baseline period (937 ± 242 ms) than during nitroprusside infusion (812 ± 213 ms, $p < 0.0002$). The right ventricular effective refractory period measured at the apex was encountered before induction of an arrhythmia during both trials of programmed stimulation in 10 patients at a ventricular drive train cycle length 600 ms and in 7 patients at a drive train cycle length 400 ms. At a ventricular drive train cycle length of 600 ms, the mean effective refractory period during the baseline (271 ± 30 ms) and nitroprusside infusion (274 ± 31 ms) periods was similar. Baseline mean effective refractory period at a drive train cycle length of 400 ms (249 ± 25 ms) also did not significantly change during nitroprusside infusion (246 ± 18 ms).

Response to programmed cardiac stimulation (Table 4). Two patients (Patients 4 and 8) had no ventricular tachycardia induced during either the baseline period or during nitroprusside infusion (Fig. 1). In the remaining 10 patients, ventricular tachyarrhythmias were induced from the right ventricular apex during both periods. Sustained ventricular tachycardia was induced in eight patients, and nonsustained ventricular tachycardia was reproducibly induced in one patient during both study periods. In one patient, sustained ventricular tachycardia was induced during the baseline period and ventricular fibrillation during nitroprusside infusion. Thus, the response to programmed cardiac stimulation during the two periods differed in only one (8%) of the patients. This patient was taking sotalol at the time of study, and had hemodynamic changes during nitroprusside infusion similar to those of the other patients.

The mean number of extrastimuli required to induce ventricular tachyarrhythmia was similar during the baseline period (1.8 ± 0.6) and during nitroprusside infusion (1.9 ± 0.7). In seven patients, equal numbers of ventricular extrastimuli induced a tachyarrhythmia during the two programmed stimulations. Two patients required one more and one patient required one less extrastimulus to induce ventricular tachycardia during nitroprusside infusion.

For the nine patients in whom ventricular tachycardia was induced during both trials of programmed stimulation, the mean tachycardia cycle length was 347 ± 61 ms during the baseline period and 342 ± 70 ms during nitroprusside infusion (p = NS) (Fig. 2). The surface ECG configuration of the two ventricular tachycardias induced at baseline and during nitroprusside infusion was similar in six patients. In three patients, morphologically different ventricular tachycardias were induced during the two programmed stimulation periods.

Discussion

This study evaluates the effects of acute hemodynamic improvement on several electrophysiologic variables and on the characteristics of ventricular tachycardia induction in patients with left ventricular dysfunction and ventricular tachycardia due to coronary artery disease. Intravenous nitroprusside administered in doses sufficient to improve hemodynamic variables and significantly decrease left ventricular size failed to change the right ventricular effective refractory period and did not affect characteristics of ventricular tachycardia induction during antiarrhythmic drug therapy. Ventricular tachycardias induced during nitroprusside infusion were similar in cycle length and, in most cases, in surface ECG configuration to those induced in the baseline state.

Previous studies. Studies (10–16) of isolated cardiac tissue, isolated heart preparations and intact animals have suggested an association between cardiac mechanical and electrophysiologic properties. Spear and Moore (11) demon-

Table 4. Electrophysiologic Measurements in 12 Patients

Patient No.	Study Period	SCL (ms)	RV ERP at Drive Train CL (ms)		Induced Arrhythmia	Arrhythmia CL (ms)	No. of Extrastimuli	VT Configuration in the Two Study Periods
			600	400				
1	B	810			NSVT	400	1	
	N	700			NSVT	400	2	Same
2	B	800	230		VT	320	1	
	N	680	240		VT	320	1	Different
3	B	780	250	220	VT	340	2	
	N	760	250	240	VT	325	2	Same
4	B	1000	310	290	NIA			
	N	870	300	270	NIA			
5	B	970	260		VT	360	2	
	N	700	260		VT	360	1	Same
6	B	860			VT	240	3	
	N	680			VT	210	3	Different
7	B	800	250	250	VT	430	2	
	N	730	260	230	VT	420	3	Same
8	B	800	260	220	NIA			
	N	680	260	220	NIA			
9	B	1350	260	250	VT	280	2	
	N	1250	270	240	VF		2	
10	B	770	270	240	VT	280	2	
	N	650	270	260	VT	270	2	Same
11	B	800	290	270	VT	350	2	
	N	800	280	260	VT	350	2	Same
12	B	1500	330		VT	400	1	
	N	1250	350		VT	420	1	Different
Mean ± SD	B	937 ± 242	271 ± 30	249 ± 25		347 ± 61	1.8 ± 0.6	
	N	812 ± 213	274 ± 31	246 ± 18		342 ± 70	1.9 ± 0.7	
p<		0.0002	NS	NS		NS	NS	

CL = cycle length; NIA = no inducible arrhythmia; NSVT = nonsustained ventricular tachycardia; RV ERP = right ventricular effective refractory period; SCL = sinus cycle length; VF = ventricular fibrillation; VT = ventricular tachycardia; other abbreviations as in Table 1.

strated that alterations in the action potential of mammalian myocardium result from alterations in contractile force. Other investigators (10,13) have shown that myocardial stretch during diastole can cause rest membrane potential depolarization, which, in turn, may generate premature action potentials. Changes in action potential amplitude, action potential duration and conduction velocity have been noted as a result of stretch applied to myocardium (12,14,15). Recently, Gornick et al. (16), using an open chest canine model, demonstrated that late diastolic papillary muscle traction during atrial pacing was associated with earlier local ventricular activation, altered QRS configuration and prolongation of the relative refractory period. In a canine model of recent myocardial infarction, Tobler et al. (23) demonstrated changes in the ventricular effective refractory period near the infarct border zone during transient aortic occlusion. Calkins et al. (24) noted a reduction in the absolute refractory period when left ventricular volume was

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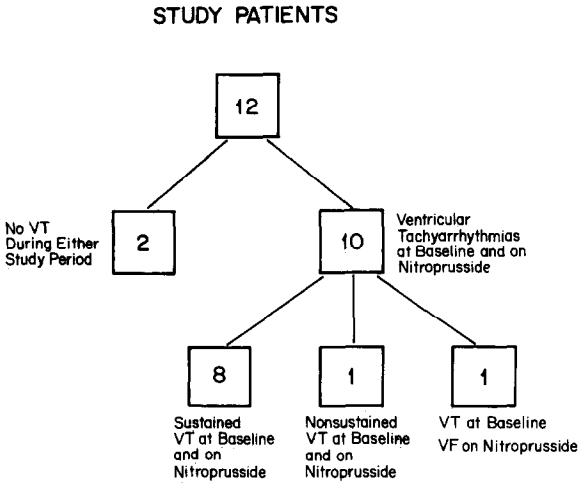
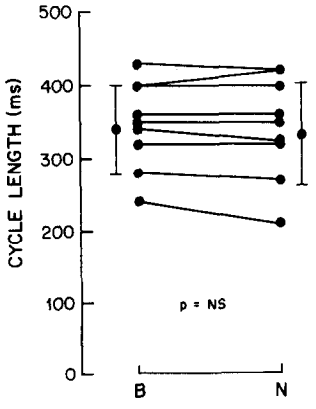


Figure 1. Results of electrophysiologic study at baseline and during nitroprusside infusion in the 12 study patients. Of the 12 patients, 10 had induction of either ventricular tachycardia (VT) or ventricular fibrillation (VF) during both study periods.

increased in the chronically infarcted canine heart. These results suggest that acute changes in left ventricular wall tension may affect impulse generation and propagation, refractoriness and, in turn, arrhythmogenesis.

Effects of acute hemodynamic improvement in humans. Several clinical studies (2,4–7) have demonstrated an association between the severity of congestive heart failure and the frequency and severity of ventricular arrhythmias. If increased wall tension is a significant proarrhythmic factor in cardiomegaly, decreasing chamber size and wall tension would be expected to decrease the incidence of arrhythmias. Although this hypothesis has never been tested directly, a reduction in ventricular ectopic activity has been noted during long-term treatment of patients with heart failure with either captopril (19) or enalapril (20). Two studies, V-HEFT1

Figure 2. Ventricular tachycardia cycle length at baseline (B) study and during nitroprusside (N) infusion for the nine patients with ventricular tachycardia during both study periods.



(17) and CONSENSUS (18), demonstrated a reduced mortality rate when hydralazine and isosorbide dinitrate, or enalapril, respectively, were added to the therapy of patients with heart failure. In the CONSENSUS study (18), however, the improved mortality rate was limited to that due to hemodynamic deterioration; no change in the incidence of sudden death was noted in patients taking enalapril.

In our study, the influence of the hemodynamic effect of nitroprusside on left ventricular size was demonstrated by a 3% to 7% decrease in ventricular linear dimension and a 7% to 19% decrease in cross-sectional area (Table 3). These figures correspond approximately to the 13% reduction in ventricular volume resulting from nitroprusside infusion reported in a previous study (25) of patients with heart failure. This hemodynamic improvement did not, however, affect the right ventricular effective refractory period or the response to programmed cardiac stimulation. These findings suggest that, in patients with coronary artery disease and left ventricular dysfunction, acute hemodynamic improvement does not alter the substrate responsible for the initiation and maintenance of sustained ventricular tachycardia.

Influence of catecholamines. Experimental and clinical observations have implicated catecholamines in the pathogenesis of ventricular arrhythmias in heart failure. In dogs, exogenous catecholamines decrease the ventricular effective refractory period, and sympathetic stimulation may cause temporal dispersion in recovery of myocardial excitability, effects that may predispose to arrhythmias (26). Isoproterenol administered during programmed cardiac stimulation may facilitate induction of ventricular tachycardia (27,28). Morady et al. (29) found that plasma norepinephrine concentrations increased, but that plasma epinephrine concentrations did not change during induction of ventricular tachycardia. Increases in plasma norepinephrine, however, were not associated with changes in the ventricular effective refractory period or characteristics of ventricular tachycardia induction. In our study, plasma norepinephrine concentration was higher during nitroprusside infusion than during the baseline period, whereas epinephrine concentration was unchanged. Nitroprusside infusion caused a significant decrease in sinus cycle length, but not in the ventricular refractory period, presumably because of a greater sympathetic influence on the sinus node than on the myocardium. Nevertheless, the possibility that an increase in plasma norepinephrine concentration counteracted a potential beneficial effect of nitroprusside infusion in suppressing ventricular tachycardia cannot be excluded.

Limitations of the study. Several limitations of our study should be considered. First, this study was conducted in a small, homogeneous and selected group of patients; all had left ventricular dysfunction due to coronary artery disease and all responded to baseline programmed stimulation with sustained monomorphic ventricular tachycardia. Therefore, our results cannot be generalized to patients with compara-

ble left ventricular dysfunction but without coronary artery disease. Furthermore, in patients with left ventricular dysfunction of any cause, the baseline response to programmed cardiac stimulation may be nonsustained ventricular tachycardia or ventricular fibrillation rather than sustained monomorphic ventricular tachycardia; in these patients, unlike our study group, the response to programmed stimulation might be influenced by changes in hemodynamic variables. Thus, our findings can not be generalized to patients in whom the response to programmed stimulation is different from sustained monomorphic ventricular tachycardia.

Second, all 12 patients were receiving antiarrhythmic drug therapy at the time of study. Our inclusion criteria did not require persistent presence of induced ventricular tachycardia with antiarrhythmic drug therapy, as evident from the inclusion of the two patients with no induced tachycardia on such therapy. However, because inducible ventricular tachycardia persisted in the majority (83%) of the patients, our study predominantly investigated the effect of hemodynamic improvement on persistently inducible ventricular tachycardia in patients being treated with antiarrhythmic drugs. Our results, therefore, cannot be generalized to patients who are not taking such drugs.

A more technical limitation involves the ventricular effective refractory period, which was measured at the right ventricular apex. In previous studies (23,24), the effects of hemodynamic changes on ventricular refractoriness were greatest in or near infarcted tissue. Our study does not exclude possible substantial changes in the myocardial effective refractory period at sites other than the right ventricular apex, particularly those in the infarct border zone.

Although all of the patients had depressed left ventricular ejection fraction, none had clinically decompensated heart failure at the time of study. The baseline filling pressures observed in our study may not have been elevated sufficiently to affect electrophysiologic variables. Therefore, we cannot exclude the possibility that patients with decompensated heart failure would demonstrate changes in electrophysiologic variables during nitroprusside infusion. To effect a small change in ventricular refractoriness, Calkins et al. (24) increased left ventricular volume by >100%. In the study by Tobler et al. (23), peak left ventricular systolic pressure increased by 93 ± 28 mm Hg. Changes in hemodynamic variables in our study did not approach the magnitude of the changes in either of these studies. However, induction of ventricular tachycardia did not change, even in the six patients whose baseline mean pulmonary capillary wedge pressure was >20 mm Hg. These data are consistent with the preliminary data of Kulick et al. (30), who studied patients with dilated cardiomyopathy in hemodynamically decompensated and compensated (with nitroprusside) states. They demonstrated no differences between the two states in right ventricular effective refractory period or inducibility of ventricular tachyarrhythmias. However, their patients were different from ours in that they had not previously had spontaneous sustained ventricular tachycardia.

Finally, in patients with heart failure, long-term rather than short-term hemodynamic improvement may be required to alter the electrophysiologic characteristics of the diseased myocardium and ventricular tachycardia induction characteristics. Experimental observations by Pfeffer et al. (31), who showed that long-term treatment with vasodilators decreased left ventricular remodeling and improved left ventricular performance after myocardial infarction in rats, may be applicable to other species as well and may be relevant to long-term changes in electrophysiologic characteristics of the myocardium. Modulation of electrophysiologic variables associated with these changes in cardiac volume and geometry may also occur only after long-term vasodilator therapy.

Conclusions. From our data, we conclude that, in patients receiving antiarrhythmic drug therapy for ventricular tachycardia associated with left ventricular dysfunction and coronary artery disease, short-term hemodynamic improvement does not result in a concomitant beneficial electrophysiologic effect on the induction characteristics of ventricular tachycardia. Determination of whether long-term vasodilator therapy affects ventricular tachycardia induction requires further study.

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